

PRELIMINARY AMENDMENT

U.S. Appln. No. 09/368,866

substituted with C₁₋₆ alkyl; C₁₋₆ alkoxy; C₁₋₆ alkanoyl; hydroxy; hydroxyalkyl; halo; haloalkyl; nitro; cyano; cyanoalkyl; amino optionally substituted with C₁₋₆ alkyl; amido; or (lower alkyl)amide; or **B** is an acyl derivative of formula **R**₄-C(O)-; a carboxyl of formula **R**₄-O-C(O)-; an amide of formula **R**₄-N(**R**₅)-C(O)-; a thioamide of formula **R**₄-N(**R**₅)-C(S)-; or a sulfonyl of formula **R**₄-SO₂ wherein

R₄ is (i) C₁₋₁₀ alkyl optionally substituted with carboxyl, C₁₋₆ alkanoyl, hydroxy, C₁₋₆ alkoxy, amino optionally mono- or di-substituted with C₁₋₆ alkyl, amido, or (lower alkyl) amide; (ii) C₃₋₇ cycloalkyl, C₃₋₇ cycloalkoxy, or C₄₋₁₀ alkylcycloalkyl, all optionally substituted with hydroxy, carboxyl, (C₁₋₆ alkoxy)carbonyl, amino optionally mono- or di-substituted with C₁₋₆ alkyl, amido, or (lower alkyl) amide; (iii) amino optionally mono- or di-substituted with C₁₋₆ alkyl; amido; or (lower alkyl)amide; (iv) C₆ or C₁₀ aryl or C₇₋₁₆ aralkyl, all optionally substituted with C₁₋₆ alkyl, hydroxy, amido, (lower alkyl)amide, or amino optionally mono- or di-substituted with C₁₋₆ alkyl; or (v) Het or (lower alkyl)-Het, both optionally substituted with C₁₋₆ alkyl, hydroxy, amido, (lower alkyl) amide, or amino optionally mono- or di-substituted with C₁₋₆ alkyl; **R**₅ is H or C₁₋₆ alkyl; with the proviso that when **R**₄ is an amide or a thioamide, **R**₄ is not (ii) a cycloalkoxy;

Y is H or C₁₋₆ alkyl;

R³ is C₁₋₈ alkyl, C₃₋₇ cycloalkyl, or C₄₋₁₀ alkylcycloalkyl, all optionally substituted with hydroxy, C₁₋₆ alkoxy, C₁₋₆ thioalkyl, amido, (lower alkyl)amido, C₆ or C₁₀ aryl, or C₇₋₁₆ aralkyl;

[R₂] **R**² is CH₂-**R**₂₀, NH-**R**₂₀, O-**R**₂₀ or S-**R**₂₀, wherein **[R**₂₀ is a saturated or unsaturated C₃₋₇ cycloalkyl or C₄₋₁₀ (alkylcycloalkyl), all of which being optionally mono-, di- or tri-substituted with **R**₂₁,

or **R**₂₀ is a C₆ or C₁₀ aryl or C₇₋₁₄ aralkyl, all optionally mono-, di- or tri-substituted with **R**₂₁, or] **R**₂₀ is [Het or (lower alkyl)-Het] pyridinyl, quinolyl, (lower alkyl)-pyridinyl or (lower alkyl)-quinolyl, [both] each optionally mono-, di- or tri-substituted with **R**₂₁,

wherein each **R**₂₁ is independently C₁₋₆ alkyl; C₁₋₆ alkoxy; lower thioalkyl; sulfonyl; NO₂; OH; SH; halo; haloalkyl; amino optionally mono- or di-substituted with C₁₋₆ alkyl, C₆ or

PRELIMINARY AMENDMENT
U.S. Appln. No. 09/368,866

A1
C₁₀ aryl, C₇₋₁₄ aralkyl, Het or (lower alkyl)-Het; amido optionally mono-substituted with C₁₋₆ alkyl, C₆ or C₁₀ aryl, C₇₋₁₄ aralkyl, Het or (lower alkyl)-Het; carboxyl; carboxy(lower alkyl); C₆ or C₁₀ aryl, C₇₋₁₄ aralkyl or Het, said aryl, aralkyl or Het being optionally substituted with R₂₂;

wherein R₂₂ is C₁₋₆ alkyl; C₃₋₇ cycloalkyl; C₁₋₆ alkoxy; amino optionally mono- or di-substituted with C₁₋₆ alkyl; sulfonyl; (lower alkyl)sulfonyl; NO₂; OH; SH; halo; haloalkyl; carboxyl; amide; (lower alkyl)amide; or Het optionally substituted with C₁₋₆ alkyl;

R¹ is H; C₁₋₆ alkyl, C₃₋₇ cycloalkyl, C₂₋₆ alkenyl, or C₂₋₆ alkynyl, all optionally substituted with halogen;

or a pharmaceutically acceptable salt or ester thereof;

wherein "Het" is defined as a five-membered saturated or unsaturated, including aromatic,

heterocycle containing from one to four heteroatoms selected from nitrogen, oxygen and sulfur,

wherein said heterocycle is optionally fused to a benzene ring.

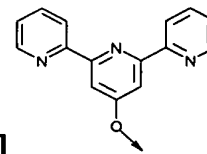
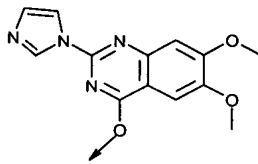
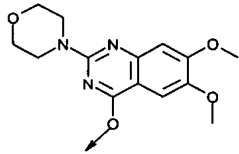
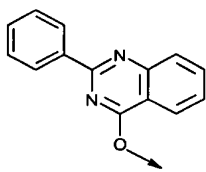
- A2
21. (amended) A compound of formula I according to claim 1, wherein [R₂] R² is S-R₂₀ or O-R₂₀ wherein R₂₀ is a [C₆ or C₁₀ aryl, C₇₋₁₆ aralkyl, Het or -CH₂-Het] pyridinyl, quinolyl, -CH₂-pyridinyl or -CH₂-quinolyl, all optionally mono-, di- or tri-substituted with R₂₁, wherein

R₂₁ is C₁₋₆ alkyl; C₁₋₆ alkoxy; lower thioalkyl; amino or amido optionally mono- or di-substituted with C₁₋₆ alkyl, C₆ or C₁₀ aryl, C₇₋₁₆ aralkyl, Het or (lower alkyl)-Het; NO₂; OH; halo; trifluoromethyl; carboxyl; C₆ or C₁₀ aryl, C₇₋₁₆ aralkyl, or Het, said aryl, aralkyl or Het being optionally substituted with R₂₂, wherein

R₂₂ is C₁₋₆ alkyl; C₃₋₇ cycloalkyl; C₁₋₆ alkoxy; amino; mono- or di-(lower alkyl)amino; (lower alkyl)amide; sulfonylalkyl; NO₂; OH; halo; trifluoromethyl; carboxyl or Het.

- A3
25. (amended) A compound of formula I according to claim 21, wherein [R₂] R² is [selected from the group consisting of:

PRELIMINARY AMENDMENT
U.S. Appln. No. 09/368,866



26. (amended) A compound of formula I according to claim 21, wherein $[R_2]$ R^2 is [1-naphthylmethoxy; 2-naphthylmethoxy; benzyloxy, 1-naphthoxy; 2-naphthoxy; or] quinolinoxy unsubstituted, mono- or di-substituted with R_{21} as defined in claim 21.

Please cancel claim 27.

In claim 28, line 1, delete "27" and insert --26--, and delete " R_2 " and insert -- R^2 --.

In claim 29, line 1, delete " R_2 " and insert -- R^2 --.

In claims 32 and 33, line 1 of each, delete " R_2 " and insert -- R^2 --.

In the following claims, delete " R_1 " and insert -- R^1 --:

Claim 36, line 2; Claim 38, line 1; Claim 39, line 1 and line 3 (in the structures); Claim 40, line 1 and line 3 (in the structures); Claim 42, line 1 and line 3 (in the structure); Claim 43, line 1; Claim 44, line 1.

45. (amended) A compound of formula I according to claim 1, wherein

B is a C_6 or C_{10} aryl or C_{7-16} aralkyl, all optionally substituted with C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} alkanoyl, hydroxy, hydroxyalkyl, halo, haloalkyl, nitro, cyano, cyanoalkyl, amido, (lower alkyl)amido, or amino optionally substituted with C_{1-6} alkyl; or

Het or (lower alkyl)-Het, all optionally substituted with C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} alkanoyl, hydroxy, hydroxyalkyl, halo, haloalkyl, nitro, cyano, cyanoalkyl, amido, (lower alkyl)amido, or

PRELIMINARY AMENDMENT
U.S. Appln. No. 09/368,866

amino optionally substituted with C₁₋₆ alkyl, or

B is R₄-SO₂ wherein R₄ is preferably amido; (lower alkyl)amide; C₆ or C₁₀ aryl, C₇₋₁₄ aralkyl or Het, all optionally substituted with C₁₋₆ alkyl, or

B is an acyl derivative of formula R₄-C(O)- wherein R₄ is

- AY
- (i) C₁₋₁₀ alkyl optionally substituted with carboxyl, hydroxy or C₁₋₆ alkoxy, amido, (lower alkyl)amide, or amino optionally mono- or di-substituted with C₁₋₆ alkyl;
 - (ii) C₃₋₇ cycloalkyl or C₄₋₁₀ alkylcycloalkyl, both optionally substituted with hydroxy, carboxyl, (C₁₋₆ alkoxy)carbonyl, amido, (lower alkyl)amide, or amino optionally mono- or di-substituted with C₁₋₆ alkyl;
 - (iv) C₆ or C₁₀ aryl or C₇₋₁₆ aralkyl, all optionally substituted with C₁₋₆ alkyl, hydroxy, amido, (lower alkyl)amide, or amino optionally substituted with C₁₋₆ alkyl;
 - (v) Het or (lower alkyl)-Het, both optionally substituted with C₁₋₆ alkyl, hydroxy, amino optionally substituted with C₁₋₆ alkyl, amido, (lower alkyl)amide, or amino optionally substituted with C₁₋₆ alkyl, or

B is a carboxyl of formula R₄-O-C(O)-, wherein R₄ is

- (i) C₁₋₁₀ alkyl optionally substituted with carboxyl, C₁₋₆ alkanoyl, hydroxy, C₁₋₆ alkoxy, amino optionally mono- or di-substituted with C₁₋₆ alkyl, amido or (lower alkyl)amide;
- (ii) C₃₋₇ cycloalkyl, C₄₋₁₀ alkylcycloalkyl, all optionally substituted with carboxyl, (C₁₋₆ alkoxy)carbonyl, amino optionally mono- or di-substituted with C₁₋₆ alkyl, amido or (lower alkyl)amide;
- (iv) C₆ or C₁₀ aryl or C₇₋₁₆ aralkyl optionally substituted with C₁₋₆ alkyl, hydroxy, amido, (lower alkyl)amido, or amino optionally mono- or di-substituted with C₁₋₆ alkyl; or
- (v) Het or (lower alkyl)-Het, both optionally substituted with C₁₋₆ alkyl, hydroxy, amino optionally mono- or di-substituted with C₁₋₆ alkyl, amido or (lower alkyl)amido, or

B is an amide of formula R₄-N(R₅)-C(O)- wherein R₄ is

- (i) C₁₋₁₀ alkyl optionally substituted with carboxyl, C₁₋₆ alkanoyl, hydroxy, C₁₋₆ alkoxy, amido, (lower alkyl)amido, or amino optionally mono- or di-substituted with C₁₋₆ alkyl;
- (ii) C₃₋₇ cycloalkyl or C₄₋₁₀ alkylcycloalkyl, all optionally substituted with carboxyl, (C₁₋₆

PRELIMINARY AMENDMENT

U.S. Appln. No. 09/368,866

alkoxy)carbonyl, amido, (lower alkyl)amido, or amino optionally mono- or di-substituted with C₁₋₆ alkyl;

(iii) amino optionally mono- or di-substituted with C₁₋₃ alkyl;

(iv) C₆ or C₁₀ aryl or C₇₋₁₆ aralkyl, all optionally substituted with C₁₋₆ alkyl, hydroxy, amido, (lower alkyl)amide, or amino optionally substituted with C₁₋₆ alkyl; or

(v) Het or (lower alkyl)-Het, both optionally substituted with C₁₋₆ alkyl, hydroxy, amino optionally substituted with C₁₋₆ alkyl, amido or (lower alkyl)amide; and

R₅ is H or methyl, or

B is thioamide of formula R₄-NH-C(S)-; wherein R₄ is

(i) C₁₋₁₀ alkyl optionally substituted with carboxyl, C₁₋₆ alkanoyl or C₁₋₆ alkoxy;

(ii) C₃₋₇ cycloalkyl or C₄₋₁₀ alkylcycloalkyl, all optionally substituted with carboxyl, (C₁₋₆ alkoxy)carbonyl, amino or amido;

AY Y is H or methyl;

R³ is C₁₋₈ alkyl, C₃₋₇ cycloalkyl, or C₄₋₁₀ alkylcycloalkyl, all optionally substituted with hydroxy, C₁₋₆ alkoxy, C₁₋₆ thioalkyl, acetamido, C₆ or C₁₀ aryl, or C₇₋₁₆ aralkyl;

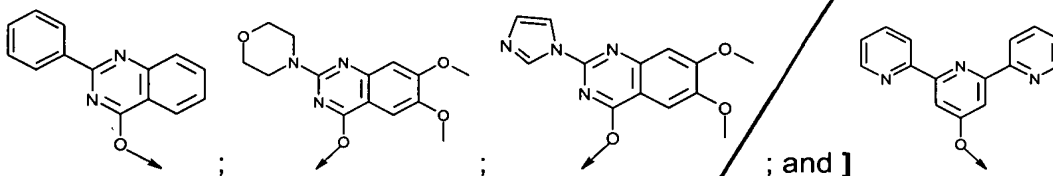
[R₂] R² is S-R₂₀ or O-R₂₀ wherein R₂₀ is [preferably a C₆ or C₁₀ aryl, C₇₋₁₆ aralkyl, Het or -CH₂-Het] pyridinyl, quinolyl, -CH₂-pyridinyl or -CH₂-quinolyl, all optionally mono-, di- or tri-substituted with R₂₁, wherein

R₂₁ is C₁₋₆ alkyl; C₁₋₆ alkoxy; lower thioalkyl; amino or amido optionally mono- or di-substituted with C₁₋₆ alkyl, C₆ or C₁₀ aryl, C₇₋₁₆ aralkyl, Het or (lower alkyl)-Het; NO₂; OH; halo; trifluoromethyl; carboxyl; C₆ or C₁₀ aryl, C₇₋₁₆ aralkyl, or Het, said aryl, aralkyl or Het being optionally substituted with R₂₂, wherein

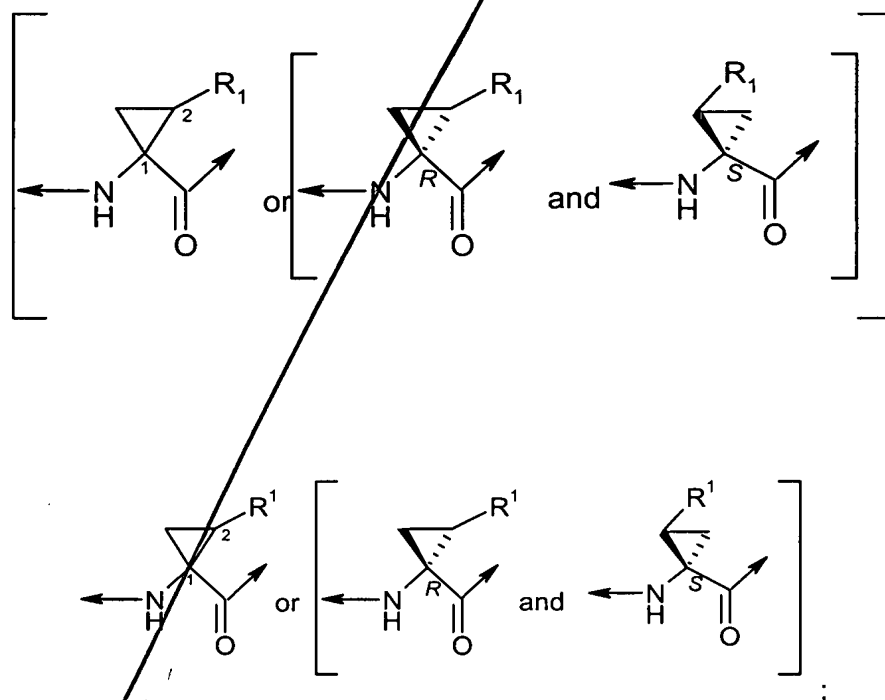
R₂₂ is C₁₋₆ alkyl; C₃₋₇ cycloalkyl; C₁₋₆ alkoxy; amino; mono- or di-(lower alkyl)amino; (lower alkyl)amide; sulfonylalkyl; NO₂; OH; halo; trifluoromethyl; carboxyl or Het; or

[R₂] R² is [selected from the group consisting of:

PRELIMINARY AMENDMENT
U.S. Appln. No. 09/368,866



or **[R₂]** **R²** is [1-naphthylmethoxy; 2-naphthylmethoxy; benzyloxy, 1-naphthyloxy; 2-naphthyloxy; or] quinolinoxy unsubstituted, mono- or di-substituted with **R₂₁** as defined above; and the **P1** segment is a cyclopropyl ring, both optionally substituted with **[R₁]** **R¹**, wherein **R¹** is C₁₋₃ alkyl, C₃₋₅ cycloalkyl, or C₂₋₄ alkenyl optionally substituted with halo, and said **[R₁]** **R¹** at carbon 2 is orientated *syn* to the carbonyl at position 1, represented by the radical:



or a pharmaceutically acceptable salt or ester thereof.

46. (Amended) A compound of formula I according to claim 45, wherein **B** is a C₆ or C₁₀ aryl optionally substituted with C₁₋₆ alkyl, C₁₋₆ alkoxy, C₁₋₆ alkanoyl, hydroxy, hydroxyalkyl, halo,

PRELIMINARY AMENDMENT

U.S. Appln. No. 09/368,866

haloalkyl, nitro, cyano, cyanoalkyl, amido, (lower alkyl)amide, or amino optionally mono- or di-substituted with C₁₋₆ alkyl; or **B** is Het optionally substituted with C₁₋₆ alkyl, C₁₋₆ alkoxy, C₁₋₆ alkanoyl, hydroxy, halo, amido, (lower alkyl)amide, or amino optionally mono- or di-substituted with C₁₋₆ alkyl; or

B is **R**₄-SO₂ wherein **R**₄ is C₆ or C₁₀ aryl, a C₇₋₁₄ aralkyl or Het all optionally substituted with C₁₋₆ alkyl; amido, (lower alkyl)amide; **B** is an acyl derivative of formula **R**₄-C(O)- wherein **R**₄ is

- (i) C₁₋₁₀ alkyl optionally substituted with carboxyl, hydroxy or C₁₋₆ alkoxy; or
- (ii) C₃₋₇ cycloalkyl or C₄₋₁₀ alkylcycloalkyl, both optionally substituted with hydroxy, carboxyl, (C₁₋₆ alkoxy)carbonyl; or
- (iv) C₆ or C₁₀ aryl or C₇₋₁₆ aralkyl, all optionally substituted with C₁₋₆ alkyl, hydroxy; or
- (v) Het optionally substituted with C₁₋₆ alkyl, hydroxy, amido or amino;

or **B** is a carboxyl of formula **R**₄-O-C(O)-, wherein **R**₄ is

- (i) C₁₋₁₀ alkyl optionally substituted with carboxyl, C₁₋₆ alkanoyl, hydroxy, C₁₋₆ alkoxy or amido, (lower alkyl)amide, amino optionally mono- or di-substituted with C₁₋₆ alkyl;
- (ii) C₃₋₇ cycloalkyl, C₄₋₁₀ alkylcycloalkyl, all optionally substituted with carboxyl, (C₁₋₆ alkoxy)carbonyl, amido, (lower alkyl)amide, amino optionally mono- or di-substituted with C₁₋₆ alkyl; or
- (iv) C₆ or C₁₀ aryl or C₇₋₁₆ aralkyl, all optionally substituted with C₁₋₆ alkyl, hydroxy, amino optionally substituted with C₁₋₆ alkyl; or
- (v) Het or (lower alkyl)-Het, both optionally substituted with C₁₋₆ alkyl, hydroxy, amido, or amino optionally mono-substituted with C₁₋₆ alkyl;

or **B** is an amide of formula **R**₄-N(**R**₅)-C(O)- wherein **R**₄ is

- (i) C₁₋₁₀ alkyl optionally substituted with carboxyl, C₁₋₆ alkanoyl, hydroxy, C₁₋₆ alkoxy, amido, (lower alkyl)amide, amino optionally mono- or di-substituted with C₁₋₆ alkyl;
- (ii) C₃₋₇ cycloalkyl or C₄₋₁₀ alkylcycloalkyl, all optionally substituted with carboxyl, (C₁₋₆ alkoxy)carbonyl, amido, (lower alkyl)amide, amino optionally mono- or di-substituted with C₁₋₆ alkyl; and **R**₅ is H or methyl; or

R₄ is (iii) amino optionally mono- or di-substituted with C₁₋₃ alkyl; or

PRELIMINARY AMENDMENT

U.S. Appln. No. 09/368,866

(iv) C₆ or C₁₀ aryl or C₇₋₁₆ aralkyl, all optionally substituted with C₁₋₆ alkyl, hydroxy, amino or amido optionally substituted with C₁₋₆ alkyl; or

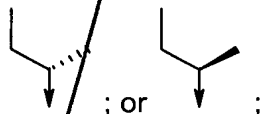
(v) Het optionally substituted with C₁₋₆ alkyl, hydroxy, amino or amido; or

B is a thioamide of formula **R₄-NH-C(S)-**; wherein **R₄** is:

(i) C₁₋₁₀ alkyl; or (ii) C₃₋₇ cycloalkyl; or

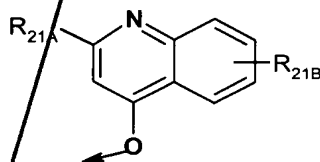
Y is H;

R³ is the side chain of *tert*-butylglycine (Tbg), Ile, Val, Chg or:



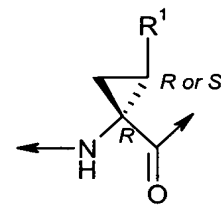
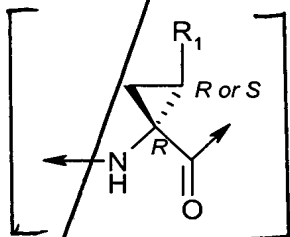
[R₂] R² is [1-naphthylmethoxy; or] quinolinoxy unsubstituted, mono- or di-substituted with **R₂₁** as defined above, or

[R₂] R² is :



wherein **R_{21A}** is C₁₋₆ alkyl; C₁₋₆ alkoxy; C₆, C₁₀ aryl or Het; lower thioalkyl; halo; amino optionally mono-substituted with C₁₋₆ alkyl; or C₆, C₁₀ aryl, C₇₋₁₆ aralkyl or Het, optionally substituted with **R₂₂** wherein **R₂₂** is C₁₋₆ alkyl, C₁₋₆ alkoxy, amido, (lower alkyl)amide, amino optionally mono- or di-substituted with C₁₋₆ alkyl, or Het;

P1 is a cyclopropyl ring wherein carbon 1 has the *R* configuration,



; and

R¹ is ethyl, vinyl, cyclopropyl, 1 or 2-bromoethyl or 1 or 2-bromovinyl.

A

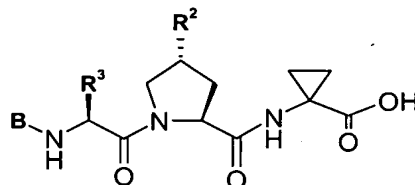
PRELIMINARY AMENDMENT

U.S. Appln. No. 09/368,866

[Claim 47, line 12, delete "R₂" and insert --R²--.

41/17 47 44 46. (amended) A compound according to claim 45 represented by the formula:

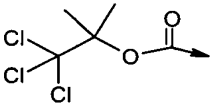
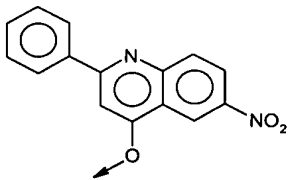
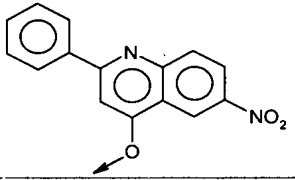
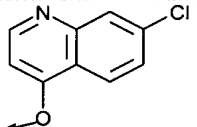
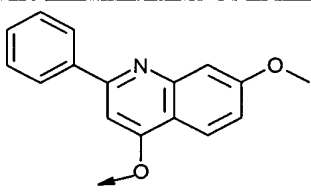
T1460



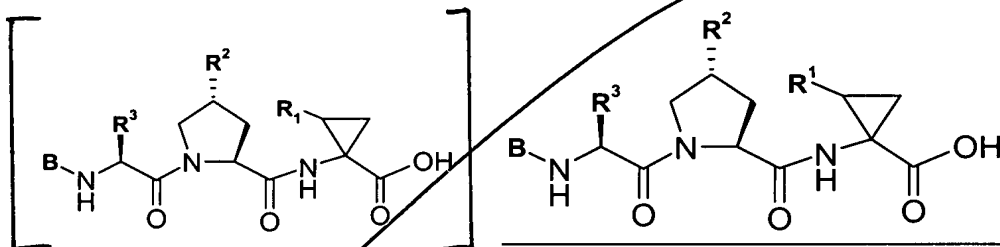
wherein B, R₃, R₂ are as defined below:

Tab 1 Cpd#	B	[R ₃]R ³	[R ₂]R ²	
[101]	Boc	cHex	-O-CH ₂ -1-naphthyl	;
102		cHex	-O-CH ₂ -1-naphthyl	;
103		cHex	-O-CH ₂ -1-naphthyl	;
104		cHex	-O-CH ₂ -1-naphthyl	;
105		cHex	-O-CH ₂ -1-naphthyl	;
106	Boc	cHex		;

PRELIMINARY AMENDMENT
U.S. Appln. No. 09/368,866

Tab 1 Cpd#	B	[R ₃]R ³	[R ₂]R ²	
[107]		cHex	-O-CH ₂ -1-naphthyl	;
108	Boc	iPr		;
109	acetyl	cHex		;
110	Boc	i-Pr		;
and 111	Boc	t-Bu		.

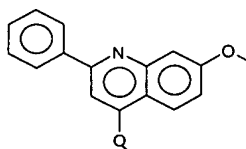
50. (amended) A compound according to claim 45 represented by the formula:



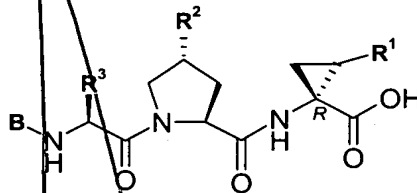
wherein B, [R₃, R₂, R₁] R³, R², R¹ are as defined below:

PRELIMINARY AMENDMENT
U.S. Appln. No. 09/368,866

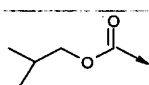
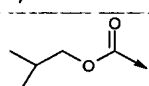
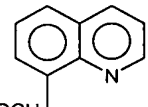
At

Table 2 Cpd #	B	[R ₃] R ³	[R ₂] R ²	[R ₁] R ¹ anti to carboxy	
[201]	Boc	cyclohexyl	-O-CH ₂ -1-naphthyl	ethyl (one isomer)	;
202	Boc	cyclohexyl	-O-CH ₂ -1-naphthyl	ethyl (other isomer)	;
and 203	Boc	<i>t</i> -Bu		vinyl 1 <i>R</i> , 2 <i>R</i>	.

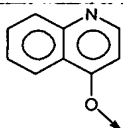
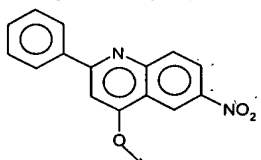
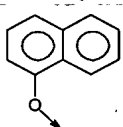
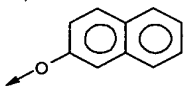
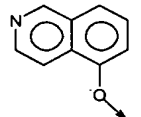
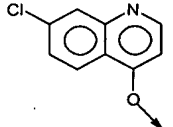
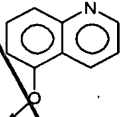
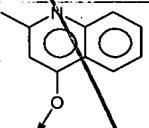
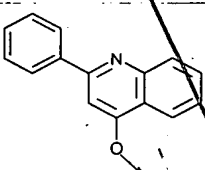
52. (amended) A compound according to claim 45 represented by the formula:



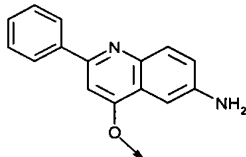
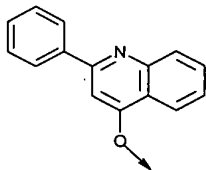
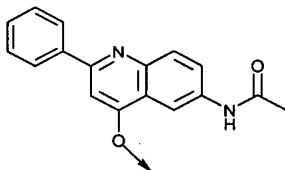
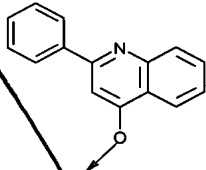
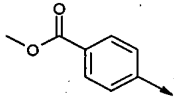
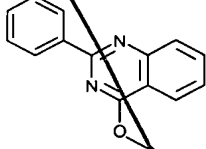
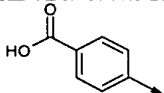
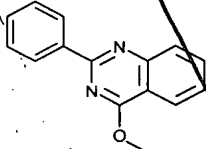
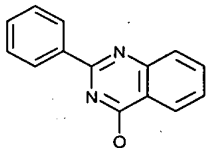
wherein B, [R₃, R₂, R₁] R³, R², R¹ are as defined below:

Table 3 Cpd #	B	[R ₃] R ³	[R ₂] R ²	[R ₁] R ¹ syn to carboxyl	
[301]	Boc	cHex	-O-CH ₂ -1-naphthyl	ethyl	;
302		iPr	-O-CH ₂ -1-naphthyl	ethyl	;
303		cHex	-O-CH ₂ -1-naphthyl	ethyl	;
304	Boc	cHex		ethyl	;
[305]	Boc	cHex	-O-CH ₂ -1-naphthyl	vinyl	;

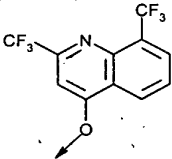
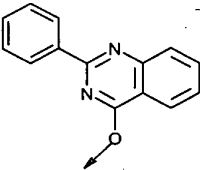

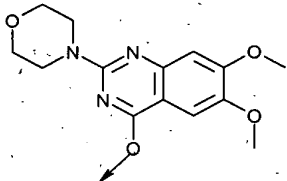
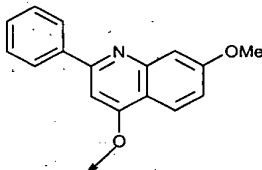

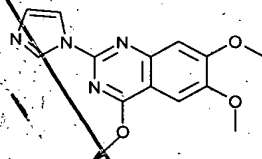
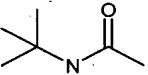
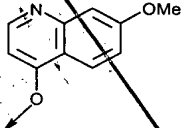
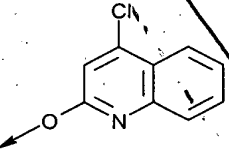
PRELIMINARY AMENDMENT
U.S. Appln. No. 09/368,866

Table 3 Cpd #	B	[R ₃]R ³	[R ₂]R ²	[R ₁] R ¹ syn to carboxyl vinyl	
306	Boc	cHex		vinyl	;
307	Boc	cHex		vinyl	;
[308]	Boc	cHex		vinyl	;
309	Boc	cHex		vinyl	;
310	Boc	cHex		vinyl	;
311	Boc	cHex		vinyl	;
312	Boc	cHex		vinyl	;
313	Boc	cHex		vinyl	;
314	Boc	cHex		vinyl	;

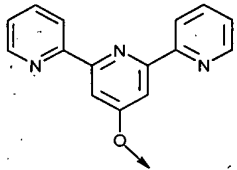
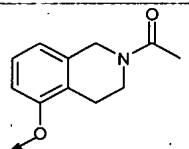
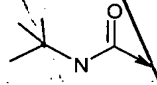
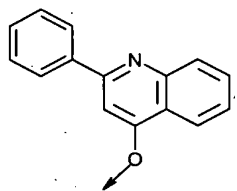
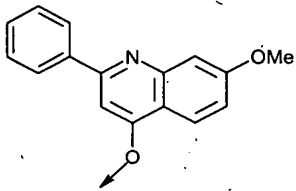
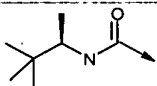
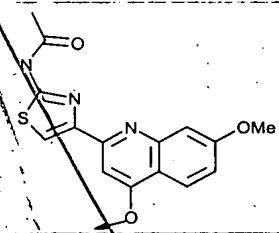
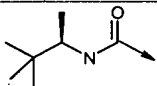
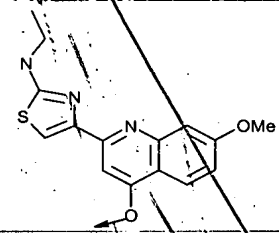
PRELIMINARY AMENDMENT
U.S. Appln. No. 09/368,866

Table 3 Cpd #	B	[R ₃]R ³	[R ₂]R ²	[R ₁] R ¹ syn to carboxyl vinyl	
315	Boc	cHex		vinyl	;
316	Acetyl	cHex		vinyl	;
317	Boc	cHex		vinyl	;
318	CF ₃ -C(O)-	<i>i</i> -Pr		vinyl	;
[319]		cHex		vinyl	;
320		cHex		vinyl	;
321	Boc	<i>t</i> -Bu		vinyl	;

PRELIMINARY AMENDMENT
U.S. Appln. No. 09/368,866

Table 3 Cpd #	B	[R ₃]R ³	[R ₂]R ²	[R ₁] R ¹ syn to carboxyl vinyl	
322	Boc	<i>t</i> -Bu		vinyl	;
[323	Boc	<i>t</i> -Bu			;
324	Boc	<i>t</i> -Bu		vinyl	;
325	Boc	<i>t</i> -Bu			;
[326	Boc	<i>t</i> -Bu		vinyl	;
327		<i>t</i> -Bu		vinyl	;
328	Boc	<i>t</i> -Bu		vinyl	;

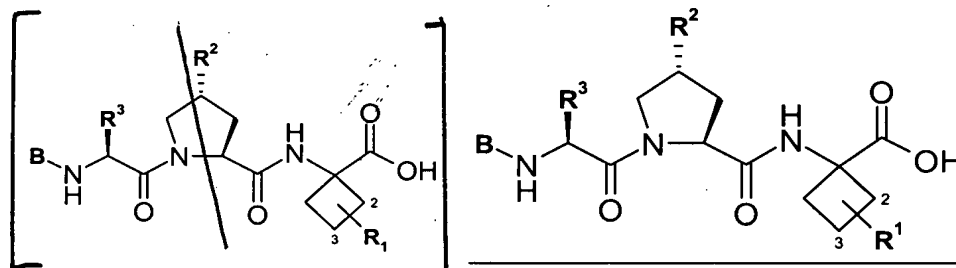
PRELIMINARY AMENDMENT
U.S. Appln. No. 09/368,866

Table 3 Cpd #	B	[R ₃]R ³	[R ₂]R ²	[R ₁] R ¹ syn to carboxyl vinyl	
329	Boc	<i>t</i> -Bu		vinyl	;
[330	Boc	<i>t</i> -Bu		vinyl	;
331		<i>t</i> -Bu		vinyl	;
332	Boc	<i>t</i> -Bu		ethyl	;
333		<i>t</i> -Bu		vinyl	;
and 334		<i>t</i> -Bu		vinyl	.

PRELIMINARY AMENDMENT
U.S. Appln. No. 09/368,866

53. (amended) A compound according to claim 52, selected from the group consisting of compound #: 307, 314, 317, [319, 321, 324,] 325, [326,] 327, 329, 331, 332, 333, and 334.

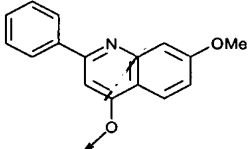
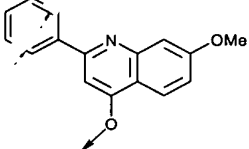
54. (amended) A compound according to claim 45 represented by the formula:



wherein B, [R₃, R₂ and R₁] R³, R² and R¹ are as defined below:

Table 4 Cpd #	B	[R ₃]R ³	[R ₂]R ²	[R ₁]R ¹
401	Boc	<i>i</i> -Pr		H ;
402	Boc	<i>t</i> -Bu		H ;
403	Boc	<i>t</i> -Bu		H ;
404	Boc	<i>t</i> -Bu		3-(=CH ₂) ;

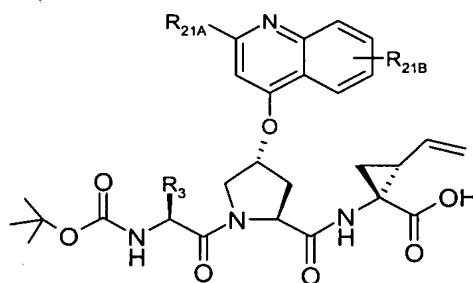
PRELIMINARY AMENDMENT
U.S. Appl. No. 09/368,866

Table 4 Cpd #	B	[R ₃]R ³	[R ₂]R ²	[R ₁]R ¹
405	Boc	<i>t</i> -Bu		2-vinyl ;
and 406	Boc	<i>t</i> -Bu		2-Et .

47

57
58.

(amended) A compound according to claim 46 represented by the formula:



wherein R₃, R_{21A} and R_{21B} are as defined below:

Table 6 Cpd #	R ₃	R _{21A}	R _{21B}
601	<i>i</i> -Pr	Ph	7-OMe ;
602	<i>t</i> -Bu	Ph	8-OMe, ; 7-OMe
603	<i>i</i> -Pr	Ph	7-ethyl ;
604	<i>t</i> -Bu	--	7-OMe ;
605	<i>t</i> -Bu	Ph	7-O- <i>i</i> Pr ;

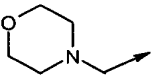
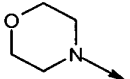
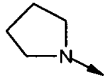
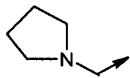
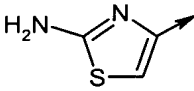
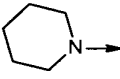
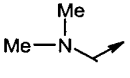
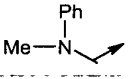
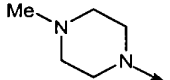
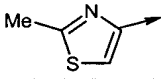
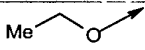
149

A

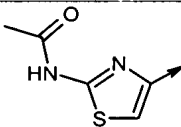
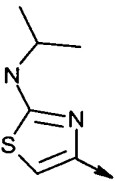
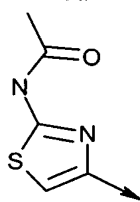
T1491

T1490

PRELIMINARY AMENDMENT
U.S. Appln. No. 09/368,866

Table 6 Cpd #	R ₃	R _{21A}	R _{21B}	
606	<i>t</i> -Bu	--	7-Cl	;
607	<i>i</i> Pr	--	7-Cl	;
608	CH ₂ - <i>i</i> Pr	--	7-Cl	;
[609	<i>t</i> -Bu		--	:]
610	<i>t</i> -Bu	Cl	--	;
611	<i>t</i> -Bu	Ph	7-N(Me) ₂	;
[612	<i>t</i> -Bu		--	:]
613	<i>t</i> -Bu		--	;
614	<i>t</i> -Bu		--	;
615	<i>t</i> -Bu	--	7-N(Me) ₂	;
616	<i>t</i> -Bu		--	;
[617	<i>t</i> -Bu		--	:]
618	<i>t</i> -Bu		--	;
619	<i>t</i> -Bu		--	;
[620	<i>t</i> -Bu		--	:]
621	<i>t</i> -Bu		--	;
622	<i>t</i> -Bu		--	;

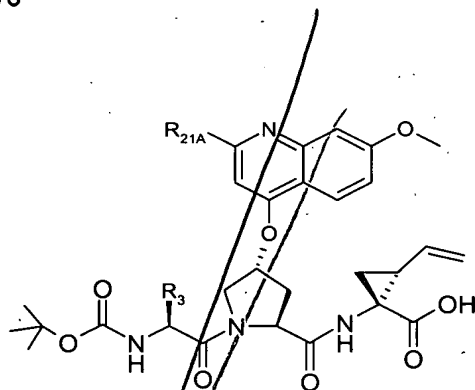
PRELIMINARY AMENDMENT
U.S. Appln. No. 09/368,866

Table 6 Cpd #	R ₃	R _{21A}	R _{21B}
623	<i>t</i> -Bu	MeO-	--
624	<i>t</i> -Bu	(Me) ₂ N-	--
625	<i>t</i> -Bu	Ph	7-S(Me)
626	<i>t</i> -Bu	Ph	7-Br
627	<i>t</i> -Bu	Ph	7-F
628	<i>t</i> -Bu		7-N(Me) ₂
629	<i>t</i> -Bu		7-N(Me) ₂
and 630	<i>t</i> -Bu		7-N(Et) ₂

58. (amended) A compound according to claim 58, selected from the group consisting of compound #:
 601, 602, 603, 604, 605, 606, 607, 610, 611, [612,] 615, 616, [617, 620,] 621, 622, 625, 626, 627,
 628, 629, and 630.

~~59. (amended) A compound according to claim 46 represented by the formula:~~

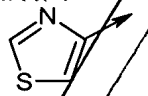
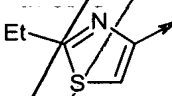
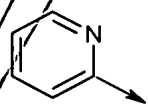
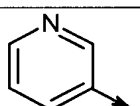
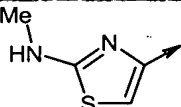
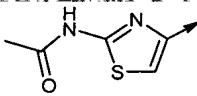
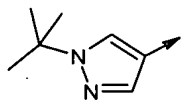
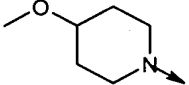
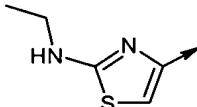
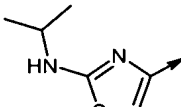
PRELIMINARY AMENDMENT
U.S. Appln. No. 09/368,866



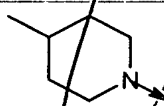
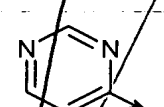
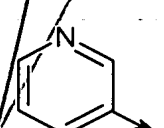
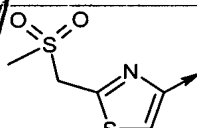
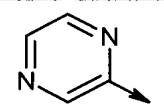
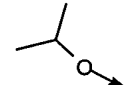
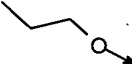
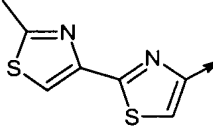
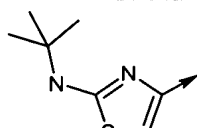
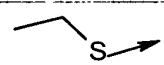
wherein R_3 and R_{21A} are as defined below:

Table 7 Cpd #	R_3	R_{21A}	
701	<i>t</i> -Bu		;
702	<i>t</i> -Bu		;
703	<i>t</i> -Bu		;
704	<i>t</i> -Bu		;
[705]	<i>t</i> -Bu		;
706	<i>t</i> -Bu		;
707	<i>t</i> -Bu		;
708	<i>t</i> -Bu	Ph-N(Me)-	;
709	<i>t</i> -Bu		;
710	<i>t</i> -Bu	HOOC-	;
711	<i>t</i> -Bu		;
712	<i>t</i> -Bu	(Me) ₂ N-	;

PRELIMINARY AMENDMENT
U.S. Appln. No. 09/368,866

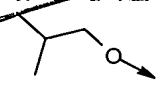
Table 7 Cpd #	R ₃	R _{21A}	
713	<i>t</i> -Bu		;
714	<i>t</i> -Bu		;
715	<i>t</i> -Bu		;
716	<i>t</i> -Bu		;
717	<i>t</i> -Bu		;
718	<i>t</i> -Bu	NH ₂	;
719	<i>t</i> -Bu		;
720	<i>t</i> -Bu		;
721	<i>t</i> -Bu		;
722	<i>t</i> -Bu		;
723	<i>t</i> -Bu		;

PRELIMINARY AMENDMENT
U.S. Appln. No. 09/368,866

Table 7 Cpd #	R ₃	R _{21A}	
[724]	<i>t</i> -Bu		;]
[725]	<i>t</i> -Bu		;]
726	<i>t</i> -Bu	<i>i</i> -Pr	;
727	<i>t</i> -Bu		;
728	<i>t</i> -Bu		;
[729]	<i>t</i> -Bu		;]
730	<i>t</i> -Bu		;
731	<i>t</i> -Bu		;
732	<i>t</i> -Bu		;
733	<i>t</i> -Bu		;
734	<i>t</i> -Bu		;

PRELIMINARY AMENDMENT
U.S. Appl. No. 09/368,866

Table 7

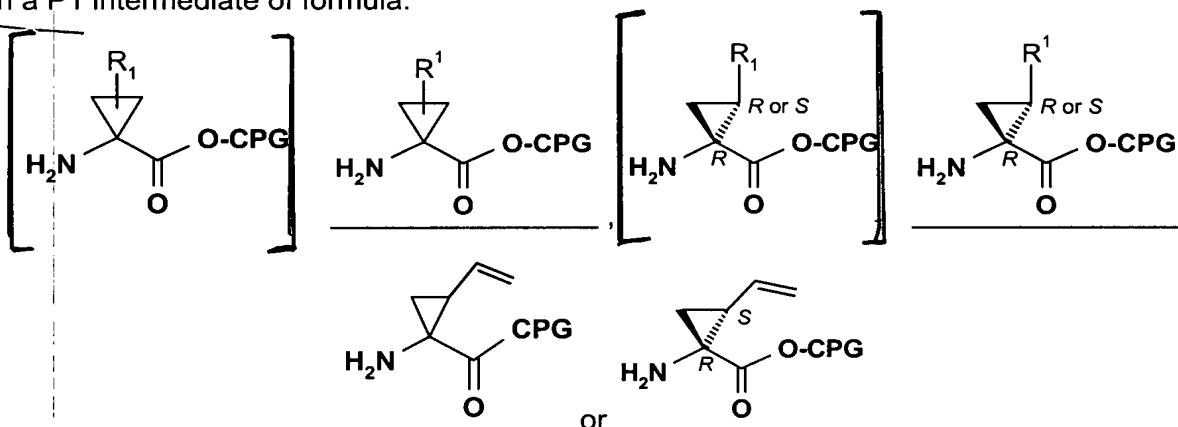
Cpd #	R ₃	R _{21A}
735	<i>t</i> -Bu	
736	<i>t</i> -Bu	<i>t</i> -Bu
and 737	<i>t</i> -Bu	CHex

61. (amended) A compound according to claim 60, selected from the group consisting of compound #: 701, 702, 703, 704, [705,] 706, 707, 708, 709, [and] 711 to 720, 722, 723, 726 to 728, and 730 to 737.

In Claims 67, 68, 69 and 70, line 1 of each claim, delete "by" and insert --comprising--.

Claim 73, line 1, after "formula (I)", insert --according to claim 1--

73. (amended) A process for the preparation of a peptide analog of formula (I) according to claim 1 wherein P1 is a substituted aminocyclopropyl carboxylic acid residue, comprising the step of:
 coupling a peptide selected from the group consisting of: APG-P3-P2; or APG-P2;
 with a P1 intermediate of formula:



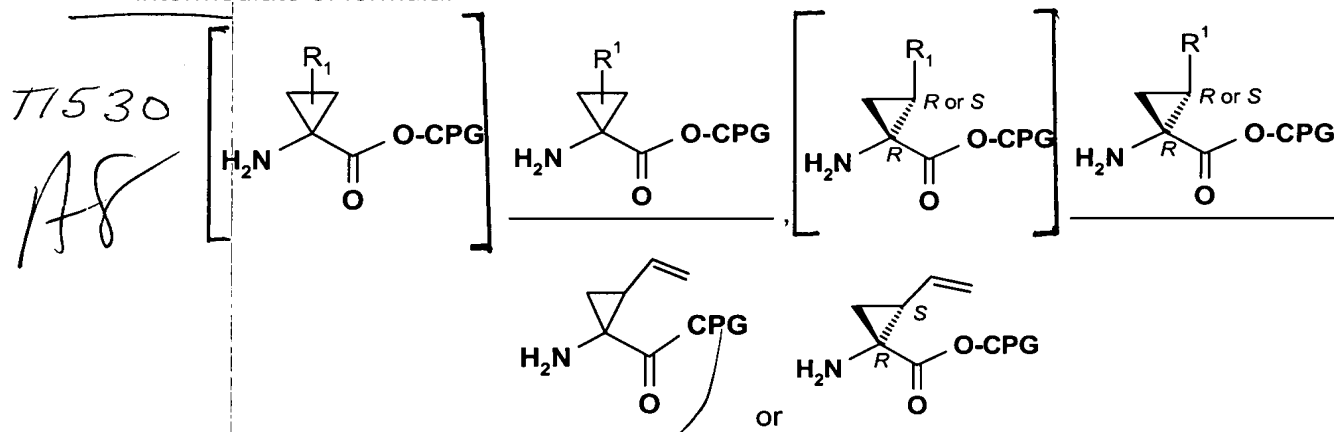
wherein [R₁]R¹ is C₁₋₆ alkyl, cycloalkyl or C₂₋₆ alkenyl, all optionally substituted with halogen,

PRELIMINARY AMENDMENT
U.S. Appln. No. 09/368,866

CPG is a carboxyl protecting group and APG is an amino protecting group and P3 and P2 are as defined above.

73
74. (amended) A process for the preparation of: [1] a serine protease inhibitor peptide analog, or 2)] a [HCV NS3 protease inhibitor] peptide analog of formula (I) according to claim 1, this process comprising the step of:

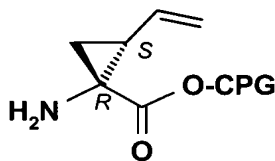
coupling a [(suitably protected)] amino acid, peptide or peptide fragment with a P1 intermediate of formula:



75. (amended) A process for the preparation of: [1] a protease inhibitor peptide analog, or 2)] a [serine protease inhibitor] peptide analog of formula (I) according to claim 1, this process comprising the step of:

coupling a [(suitably protected)] amino acid, peptide or peptide fragment with [an] a P1 intermediate of formula:

PRELIMINARY AMENDMENT
U.S. Appln. No. 09/368,866



wherein CPG is a carboxyl protecting group.

Please cancel claims 81, 82 and 83, without prejudice.

AG
84. (amended) [Use of] Method of preparing [an anti-hepatitis C virally effective amount of the compound of formula I according to claim 1, or a therapeutically acceptable salt or ester thereof for the preparation of] a composition for treating a hepatitis C viral infection in a mammal comprising combining an anti-hepatitis C virally effective amount of the compound of formula I according to claim 1, or a therapeutically acceptable salt or ester thereof, with a pharmaceutically acceptable carrier medium or auxiliary agent.

85. (amended) [Use of] Method of preparing [a hepatitis C viral NS3 protease inhibiting amount of the compound of formula I according to claim 1, or a therapeutically acceptable salt or ester thereof for the preparation of] a composition for inhibiting the replication of hepatitis C virus comprising combining a hepatitis C viral NS3 protease inhibiting amount of the compound of formula I according to claim 1, or a therapeutically acceptable salt or ester thereof, with a pharmaceutically acceptable carrier medium or auxiliary agent.

86. (amended) [Use of] Method of preparing [an anti-hepatitis C virally effective amount of a combination of the compound of formula I according to claim 1, or a therapeutically acceptable salt or ester thereof, and an interferon for the preparation of] a composition for treating a hepatitis C viral infection in a mammal comprising combining an anti-hepatitis C virally effective amount of a combination of the compound of formula I according to claim 1, or a therapeutically

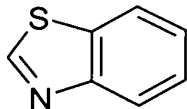
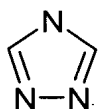
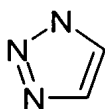
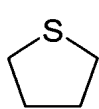
PRELIMINARY AMENDMENT
U.S. Appln. No. 09/368,866

Ag acceptable salt or ester thereof, and an interferon with a pharmaceutically acceptable carrier medium or auxiliary agent.

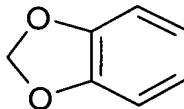
Please add the following new claim 87:

-- ~~187~~ 87. A compound of formula (I) according to claim 1, wherein each Het group is independently selected from the group consisting of pyrrolidine, tetrahydrofuran, thiazolidine, pyrrole, 1,4-dioxane, indole, or any of the following heterocycles:

T1550



or



REMARKS

The specification and claim 1 have been amended to designate the P1, P2, P3 portions of the tripeptides of formula (I) of the present invention, support being found throughout the application as filed, e.g., the synthetic methods at pages 30-34 and in claims 37, 46-47 and 73-74. This also ensures consistency within the claims.

The claims have also been amended to exclude certain subject matter that was non-elected in the Response to Restriction Requirement filed August 28, 2000. In this respect, the R₂₀ group "Het or (lower alkyl)-Het" has been amended to pyridinyl, quinolyl, (lower alkyl)-pyridinyl or (lower alkyl)-quinolyl, support being found in the pyridine and quinoline Het groups found at page 10, lines 12-13, page 18, lines 1-10, page 19, lines 8-9 and in the numerous examples throughout the application as filed.